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PATENT COOPERATION TREATY

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APR 1 2 2005

LY AND COMPANY **Patent Division**

From the INTERNATIONAL SEARCHING AUTHORITY

To: ELI LILLY AND COMPANY

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND

P.O. Box 6288 Indianapolis, IN 46206-6288 UNITED STATES OF AMERICA	THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION
	(PCT Rule 44.1)
	Date of mailing (day/month/year) 06/04/2005
Applicant's or agent's file reference	·
X-16177 🗸	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No.	International filing date
PCT/US2004/038240 🗸	(day/month/year) 10/12/2004
Applicant	
ELI LILLY AND COMPANY	

1.	x	The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.
		Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):
		When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.
		Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Fascimile No.: (41–22) 740.14.35
	•	For more detailed instructions, see the notes on the accompanying sheet.
2.		The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3.		With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
		the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
		no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4.	Rem	inders
	Shor	the after the expiration of 19 months from the priority date, the international confication will be published by the

Chortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the PCT Applicant's Guide, Volume II, National Chapters and the WIPO Internet site.

ı	Name and mailing address of the International Searching Authority	Authorized officer
	European Patent Office, P:B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Nora Hick

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international polication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been its filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
 "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
- [Where originally there were 15 claims and after amendment of all claims there are 11]:
 "Claims 1 to 15 replaced by amended claims 1 to 11."
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
 - *Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added.* or *Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged.*
- 4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

ft must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be turnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER	see Form PCT/ISA/220		
X-16177	ACTION	as well as, where applicable, item 5 below.		
International application No.	International filing date (day/mon.	h/year)	(Earliest) Priority Date (day/month/year)	
PCT/US2004/038240	10/12/2004		23/12/2003	
Applicant				
ELI LILLY AND COMPANY				
This International Search Report has bee according to Article 18. A copy is being to	n prepared by this International Sea ansmitted to the International Burea	rching Auth u.	nority and is transmitted to the applicant	
This International Search Report consists	of a total ofsh	eets.		
X It is also accompanied by	a copy of each prior art document of	cited in this	report.	
language in which it was filed, unl	ess otherwise indicated under this i	tem.	sis of the international application in the ation of the international application furnished to	
this Authority (Ru	le 23.1(b)).		in the international application, see Box No. I.	
b Whit regard to any flucter	onde andor ammo acid sequence	disclosed	in the international application, see Box No. 1.	
2. X Certain claims were fou	nd unsearchable (See Box II).			
3. Unity of invention is lac	king (see Box III).			
4. With regard to the title,				
the text is approved as su	bmitted by the applicant.			
	hed by this Authority to read as follo		•	
MORPHOLINE DERIVATIVES	AS NOREPINEPHRINE RE	UPTAKE	INHIBITORS	
	•			
•				
5. With regard to the abstract,				
X the text is approved as su	bmitted by the applicant.			
the text has been establisi may, within one month fro	hed, according to Rule 38.2(b), by the thick the date of mailing of this internation.	nis Authont ional searc	y as it appears in Box No. IV. The applicant h report, submit comments to this Authority.	
6. With regard to the drawings,			•	
a. the figure of the drawings to be p	ublished with the abstract is Figure	No		
as suggested by t				
as selected by this	s Authority, because the applicant fa	aled to sugg	gest a figure.	
	s Authority, because this figure bette	r character	izes the invention.	
b none of the figures is to be	published with the abstract.			

INTERNATIONAL SEARCH REPORT

International Application No PCT/US2004/038240

A. CLASSIFICATION OF SUBJECT MATTER
1PC 7 C07D265/30 C07D401/10 A61K31/5375 A61P25/24 A61K31/5377 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) A61K A61P CO7D Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Category ° Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. √WO 2004/018441 A (ELI LILLY AND COMPANY; P,A 1-16 CASES-THOMAS, MANUEL, JAVIER; HAUGHTON, HELEN,) 4 March 2004 (2004-03-04) abstract examples claims √WO 2004/017977 A (ELI LILLY AND COMPANY; P,A 1-16 WALTER, MAGNUS, WILHELM; CLARK, BARRY, PETER; G) 4 March 2004 (2004-03-04) abstract examples claims Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents : "T" later document published after the international filing date or pnonty date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docudocument referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 30 March 2005 06/04/2005 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx 31 651 epo nl, Fax: (+31-70) 340-3016 Stix-Malaun, E

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/038240

WO 01/01973 A (PHARMACIA & UPJOHN COMPANY; WONG, ERIK, H., F; AHMED, SAEEDUDDIN; MARS) 11 January 2001 (2001-01-11) cited in the application abstract examples claims	Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	A	WONG, ERIK, H., F; AHMED, SAEEDUDDIN; MARS) 11 January 2001 (2001-01-11) cited in the application abstract examples	1-16

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International application No. PCT/US2004/038240

INTERNATIONAL SEARCH-REPORT

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No PCT/US2004/038240

	atent document d in search report		Publication date		Patent family member(s)		Publication date
WO	2004018441	A	04-03-2004	WO	2004018441	A1	04-03-2004
WO	2004017977	Α	04-03-2004	AU	2003269923	A1	11-03-2004
			·	WO	2004017977	A2	04-03-2004
WO	0101973	Α	11-01-2001	AU	771258	B2	18-03-2004
			*	AU	5633700	Α	22-01-2001
				BR	0012136	Α	11-06-2002
	•			CA	2375908	A1	11-01-2001
				CN	1379672	Α	13-11-2002
				CZ	20014625	A3	14-08-2002
				EA	5029	B1	28-10-2004
				ΕP	1196172	A2	17-04-2002
				EP	1459748	A1	22-09-2004
				EΡ	1459749	A1	22-09-2004
			•	EP .	1459750	A1	22-09-2004
				EP	1459751	A1	22-09-2004
*				ΕP	1493442	A1	05-01-2005
			•	EP	1500395	A1	26-01-2005
				EP	1500396	A1	26-01-2005
				HU	0201623	A2	28-09-2002
				JР	2003503450	T	28-01-2003
	*			MX	PA02000562	Α	02-07-2002
			•	NO	20016406	A	19-02-2002
				NZ	515885	Α	27-08-2004
	•			PL	352252		11-08-2003
				SK	19382001		02-07-2002
				WO	0101973		11-01-2001
				US	2002061910	A1	23-05-2002
		•		US	2002086864	A1	04-07-2002
				US	2002107249	A1	08-08-2002
				US	2002128173		12-09-2002
				US	2003040464	A1	27-02-2003
		,		US	6465458		15-10-2002
				US	2004058925	A1	25-03-2004
• •				US	2004147614		29-07-2004
				ZA	200110325	Α	14-03-2003



From the

PATENT COOPERATION TREATY

INTERNATIONAL SEARCHING AUTHORITY WRITTEN OPINION OF THE see form PCT/ISA/220 INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1) 23 OCT 2005 Date of mailing X 16177 (day/month/year) see form PCT/ISA/210 (second sheet) Applicant's or agent's file reference FOR FURTHER ACTION see form PCT/ISA/220 See paragraph 2 below International application No International filing date (day/month/year) Priority date (day/month/year) PCT/US2004/038240 10.12.2004 23.12.2003 International Patent Classification (IPC) or both national classification and IPC C07D265/30, C07D401/10, A61K31/5375, A61P25/24, A61K31/5377 Applicant **ELI LILLY AND COMPANY** This opinion contains indications relating to the following items: ☑ Box No. I Basis of the opinion Box No. II ☑ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability ☐ Box No. IV Lack of unity of invention Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement Box No. VI Certain documents cited ☐ Box No. VII Certain defects in the international application ☐ Box No. VIII Certain observations on the international application **FURTHER ACTION** If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220. For further details, see notes to Form PCT/ISA/220.

<u></u>

Name and mailing address of the ISA:

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European Patent Office D-80298 Munich

Fax: +49 89 2399 - 4465

Authorized Officer

Telephone No. +49 89 2399-



10/575469 IAP9Rec'dPCT/PTO 12 APR 2006

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US2004/038240

_	Вох	No. I Basis of the opinion
1.	With the la	regard to the language, this opinion has been established on the basis of the international application in anguage in which it was filed, unless otherwise indicated under this item.
	l.	This opinion has been established on the basis of a translation from the original language into the following anguage , which is the language of a translation furnished for the purposes of international search under Rules 12.3 and 23.1(b)).
2.	With neces	regard to any nucleotide and/or amino acid sequence disclosed in the international application and ssary to the claimed invention, this opinion has been established on the basis of:
	a. typ	pe of material:
		a sequence listing
		table(s) related to the sequence listing
	b. for	mat of material:
		in written format
		in computer readable form
	c. tim	e of filing/furnishing:
		contained in the international application as filed.
		filed together with the international application in computer readable form.
		furnished subsequently to this Authority for the purposes of search.
3.	h C	n addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto las been filed or furnished, the required statements that the information in the subsequent or additional opies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4.	Additi	onal comments:
	Box I	No. II Priority
1.	d re	The validity of the priority claim has not been considered because the International Searching Authority loes not have in its possession a copy of the earlier application whose priority has been claimed or, where equired, a translation of that earlier application. This opinion has nevertheless been established on the issumption that the relevant date (Rules 43 bis.1 and 64.1) is the claimed priority date.
2.	h	this opinion has been established as if no priority had been claimed due to the fact that the priority claim as been found invalid (Rules 43 <i>bis</i> .1 and 64.1). Thus for the purposes of this opinion, the international ling date indicated above is considered to be the relevant date.
3	Δdditi	onal observations, if necessary

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US2004/038240

	x No. III Non-establishment o olicability	of op	inion with regard to novelty, inventive step and industrial
The	e questions whether the claimed rious), or to be industrially applic	invei able	ntion appears to be novel, to involve an inventive step (to be non have not been examined in respect of:
	the entire international applicat	ion,	
×	claims Nos. 15,16		
bed	cause:	•	
☒			the said claims Nos. 15,16 (Industrial applicability) relate to the not require an international preliminary examination (specify):
	see separate sheet		
	the description, claims or drawi unclear that no meaningful opin		(indicate particular elements below) or said claims Nos. are so could be formed (specify):
	the claims, or said claims Nos. could be formed.	are s	so inadequately supported by the description that no meaningful opinion
	no international search report h	as b	een established for the whole application or for said claims Nos.
	the nucleotide and/or amino aci C of the Administrative Instruct	d sed	quence listing does not comply with the standard provided for in Annex in that:
	the written form		has not been furnished
	·		does not comply with the standard
	the computer readable form		has not been furnished
	•		does not comply with the standard
			and/or amino acid sequence listing, if in computer readable form only, do ements provided for in Annex C-bis of the Administrative Instructions.
	See separate sheet for further of	detail	S

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US2004/038240

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims

1-16

No: Claims

Inventive step (IS)

Yes: Claims

1-16

No: Claims

Industrial applicability (IA)

Yes: Claims

1-14

No: Claims

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

 Certain published documents (Rules 43bis.1 and 70.10) and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

III NON-ESTABLISHMENT

Claims 15,16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

V REASONED STATEMENT

PRIOR ART

The documents cited in the International Search Report

D1: WO 01/01973 A (PHARMACIA & UPJOHN COMPANY; WONG, ERIK, H., F; AHMED, SAEEDUDDIN; MARS) 11 January 2001 (2001-01-11)

have been considered for the examination procedure.

2. NOVELTY

The subject-matter of the Claims is considered to be novel (Article 33(2) PCT). The essential structural difference between the claimed compounds and those of D1 resides in the lack of the (phenoxy)(phenyl)methyl substituent in position 2 of the morpholine unit.

3. INVENTIVE STEP

The subject-matter of the Claims appears to fulfil the requirements of Article 33(3) PCT for the following reasons:

The closest state of the art for the present application is represented by D1. D1 discloses structurally similar morpholines (see claim 13) having the same properties, namely norepinephrine reuptake inhibitors.

Therefore the problem of the present application may be seen in the provision of further morpholine derivatives acting as norepinephrine reuptake inhibitors and

being useful in the treatment of disorders such as depression.

In the light of D1 it is not obvious for the skilled person to carry out the structural modifications in order to arrive at the presently claimed structures.

It is shown in the description that tests have been carried out which proof the alleged activity.

Accordingly, inventive step can be acknowledged.

In the regional phase it might become neccessary to indicate at least one example for which a test has been carried out

4. INDUSTRIAL APPLICABILITY

For the assessment of the present Claims 14-16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

VI CERTAIN DOCUMENTS CITED

- D2: WO 2004/018441 A (ELI LILLY AND COMPANY; CASES-THOMAS, MANUEL, JAVIER; HAUGHTON, HELEN,) 4 March 2004 (2004-03-04)
- D3: WO 2004/017977 A (ELI LILLY AND COMPANY; WALTER, MAGNUS, WILHELM; CLARK, BARRY, PETER; G) 4 March 2004 (2004-03-04)

D2 and D3 might become relevant in the regional phase.

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Defects in the images include but are not limited to the items checked:
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